REMARKS

Claims 1-6, 8-56, and 59-101 were pending in the application. Claims 12-51 and 63-101 have been withdrawn from consideration. There are no amendments to the claims in the present response.

REJECTIONS WITHDRAWAN

According to the Examiner, the rejection of claims 52-56 and 59-62 under 35 U.S.C. § 112, second paragraph, and of claims 1-11 and 52-62 under 35 U.S.C. § 103(a) were withdrawn due to the amendments presented in the response filed September 8, 2009.

NON-STATUTORY OBVIOUSNESS-TYPE DOUBLE PATENTING REJECTIONS

Claims 1, 8, 9, 52, 56, 60 and 62 were rejected on the ground of non-statutory obviousness- type double patenting as being unpatentable over claims 1, 10, 13, 14, 25, 24, and 25 of U.S. Patent No: 7,384,640 in view of Argen et al. (1999, J. Immunol. 162 (2) 2432-2440; herein after "Argen").

The Examiner acknowledges that, in the response filed September 8, 2009, applicant requested that the non-statutory obviousness- type double patenting rejections be held in abeyance until patentable subject matter is determined. The Examiner cautions that the rejection will be maintained until the double patenting issue is resolved.

As before, applicant requests that these rejections be held in abeyance until patentable subject matter is determined in the present application.

35 U.S.C § 112, FIRST PARAGRAPH REJECTIONS

Claims 8, 52-56, and 59-62 were rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement.

According to the Examiner, this is a new matter rejection because neither the specification nor the originally presented claims provide support for the claims as amended in the response filed September 8, 2009. The Examiner asserts that the written description in the specification is not commensurate with the scope of the claims because the specification broadly describes immunogenic studies, but fails to set for a method of immunizing a mammalian host against disorders associated with β-amyloid protein as claimed. Applicants traverse these rejections. As indicated below, each and every aspect of the claims is

exemplified in the specification as filed and the original claims. Support for each of the elements in the claims is indicated below:

Support for an immunogenic composition comprising a cholera holotoxin (CT) and an Aβ 1-7 peptide antigen covalently associated with the CT is found, for example, page 12, lines 25 to 28, and Example 6 at pages 34 and 35.

Support for the CT in the immunogenic composition of the invention comprising an A subunit having a mutation of at least amino acid residue 29 of SEQ ID NO:2, where the mutation is not aspartic acid is found, for example at page 3, lines 11-14 of the specification as filed.

Support for the immunogenic composition of the invention additionally comprising one or more non-covalently associated Aβ 1-7 peptide antigens is found, for example in original claim 8, at page 5, line 29, and Example 9 at pages 42 and 43.

Support for a method of immunizing a mammalian host against disorders associated with β-amyloid proteins using the immunogenic compositions of the invention is found, for example at page 7, lines 21 to 27 and page 12, lines 25 to 30.

Contrary to the Examiner's assertions, the specification discloses immunogenic studies using the Aβ 1-7 peptide antigen covalently associated with a CT A comprising a mutation at amino acid 29. See for example, page 35, line 29 to page 38, line 35, which discloses parenteral immunogenicity studies using the complex, and page 39, line 1 to page 42, line 3 which discloses mucosal immunogenicity studies. Both of these examples list peptide specific IgG endpoint titers. The adjuvant activity of the complex is tested in Example 9, at page 42, line 5 to page 43, line 30. Thus, applicant submits that the specification discloses specific immunogenicity studies using the Aβ 1-7 peptide antigen covalently associated with a CT A comprising a mutation at amino acid 29.

In view of the above comments, withdrawal of the rejection under 35 U.S.C. § 112, first paragraph of claims 8, 52-56, and 59-62 is respectfully requested.

35 U.S.C § 103(a) REJECTIONS

Claims 1-5, 8-11, 52-56, and 59-62 were rejected under 35 U.S.C. § 103(a), as being unpatentable over Jobling et al (WO 00/18434, herein after referred to as "Jobling") in view of Agren et al. (1999, J. Immunol. 162:2432-2440, herein after referred to as "Agren") and Frenkel et al. (2000, PNAS 97:11455-11459, herein after referred to as "Frenkel".)

According to the Examiner, Jobling teaches an antigenic composition comprising a mutant cholera holotoxin that has reduced toxicity compared to wild-type cholera holotoxin; and the cholera holotoxin may comprise mutations at positions 7, 11, 29, 110, and 112. Jobling is further cited as teaching that the immunogenic composition comprises a diluent, a carrier, and adjuvants. The Examiner acknowledges that Jobling does not teach that the cholera toxin is covalently associated with Aβ 1-7 peptide. The Examiner cites Agren as teaching adjuvanticity of cholera holotoxin A1 subunit covalently associated to an antigen. According to the Examiner, Argen discloses that a mutated holotoxin has comparable adjuvant function to the wild type. Argen is also cited for teaching the construction of a gene fusion of the cholera toxin A1 subunit with the B cell targeting moiety from an IgG binding fragments of S. aureus protein. Frenkel is cited as teaching immunization with the Aβ 1-7 peptide antigen, and immunization protocols. (See page 14 of the Office Action.) The Examiner concludes that it would have been prima facie obvious to apply Argen's covalently associated mutant cholera holotoxin and Frenkel's Aβ 1-7 peptide antigen to Jobling's immunogenic composition to arrive at the currently claimed invention.

Applicants traverse these rejections. The claims recite an immunogenic composition comprising a cholera holotoxin (CT) covalently associated to an Aβ 1-7 peptide antigen, where the CT comprises an A subunit having a mutation of at least amino acid residue 29 of SEQ ID NO:2, where the mutation is not an aspartic acid, where the CT increases immunogenicity of the antigen.

Applicants submit that the Examination guidelines for determining obviousness under 35 U.S.C. 103 state that an obviousness rejection can not be sustained by mere conclusory statements, and list rationales that may be used to support a conclusion of obviousness. According to § 2141 from the M.P.E.P:

> " Exemplary rationales that may support a conclusion of obviousness include:
> (A) Combining prior art elements according to known methods to yield predictable results;
> (B) Simple substitution of one known element for another to obtain predictable results;
> (C) Use of known technique to improve similar devices (methods, or products) in the same way;
> (D) Applying a known technique to a known device (method, or product) ready for improvement to yield predictable results;
> (E) "Obvious to try" - choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success;

(F) Known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art;
(G) Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention. See MPEP § **2143** for a discussion of the rationales listed above along with examples illustrating how the cited rationales may be used to support a finding of obviousness. See also MPEP § **2144** - § **2144.09** for additional guidance regarding support for obviousness determinations.

Argen teaches that it is important not to use a mutated cholera holotoxin, and constructs a molecule that expresses the cholera toxin A1 subunit covalently linked to a B cell targeting moiety and demonstrates that there is no change in antigenicity. Argen asserts that the full activity of the cholera holotoxin is necessary for the adjuvant function and suggests that B cell targeting may be responsible for adjuvanticity (See abstract, first paragraph of the Discussion, and second paragraph on the left column of page 2439.).

Frenkel teaches immunization with Aβ 3-7 incorporated into the reading frame of a bacteriaphage protein. Frenkel uses free Aβ 1-7 only in a competitive inhibition experiment to characterize immune specificity of antibodies generated to the bacteriophage containing Aβ 3-7 or EFRH. Jobling teaches immunogenic compositions comprising mutant cholera toxin A1 subunits. Jobling does not suggest covalently binding the mutant holotoxin to an antigen. None of Jobling, Argen, or Frenkel teaches or suggests conjugation of a mutant holotoxin to an Aβ 1-7 peptide antigen for use in an immunogenic composition such that one of skill in the art would expect this immunogenic composition to yield predictable results.

In view of the above comments, withdrawal of the 35 U.S.C. § 103(a) obviousness rejection of claims 1-5, 8-11, 52-56, and 59-62 in view of Jobling, Agren, and Frenkel is respectfully requested.

* * * * *

CONCLUSION

In view of the above remarks Applicants respectfully submit that the Application is now in form of allowance. Allowance of the Application on the merits is respectfully requested.

A petition for a three (3) month extension of time to file this response accompanies this paper.

If any outstanding issue remains, the Examiner is invited to contact the undersigned agent at 973 660 6383 for a discussion of a mutually agreeable solution.

During the pendency of this application please treat any reply requiring a petition for extension of time for its timely submission as containing a request therefore for the appropriate length of time. Should the Commissioner determine that any fee(s) is due or that any credit for overpayment is required, the Commissioner is hereby authorized to charge any additional fee(s) and/or credit any overpayments to Deposit Account No. 01-1425. This is not an authorization to pay the issue fee.

Respectfully submitted,

Maria Restrepo-Hartwig
Agent for Applicants
Reg. No. 52,163

Wyeth LLC
Five Giralda Farms
Madison, NJ 07940
Tel. No. (973) 660-6383